

DECLARATION ABOUT OPTIONAL CORRECTION OF SLIPS IN pages 82 and 8

I, Zagzyansky Yuly, sole inventor of Application PCT/EP02/02302, make the following ~~supplement~~ corrections of slips. Slips. p.82 (lines 35-37): missed (but cited) references in Part. VI (N° 5-10). p.87 (lines 15-21): missed (but cited) References of Chapters XI and Annex IIIA. p.87 (22-39): exactly retyped "Important supplement for Search" without mention of AT Office (it was impossible alternative for ISA). [Below, see page 52 with accepted by IPEA numerous new references in Specification for my Application PCT/IB00/00843]. Paris, 11th August 2004. All pages are signed by me verso with date of 08/11/04. *Yuly Zagzyansky*

(B0000843)

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one of Art.52(3) these subject-matters (like discoveries and scientific theories) are patentable only with their applications (!). Consequently, the claims, concerning "Theory or (EVEN!) principle underlying the invention" (l'etter "T" according the Form of the EPO Research) (to see also "Guidelines.." §CII-2.2.) and claims, concerning their practical consequences must be considered ONLY ENSEMBLE, according to the law. Consequently, I present here the (priliminary) International Classification of Patents with the mentions of the corresponding claim Groups, serving to the establishment of each I.C.P. element.

Claims 1,2,3,5: H02K 44/00; G01P 3/50; G01B 11/03; G01R 5/00, 33/00; G01T 5/00; G01J 3/00. Claims 3,4,6: G01T 1/00; G01J 3/00; G21H 7/00; G21K 1/00, 7/00; G02B 23/00; G01B 15/00; G21G 1/00, 5/00. Claims 3,4,7: G01T 1/00, 7/00, 7/02, 7/04, 7/06, 3/00; G21G 1/00, 5/00; H05H 6/00; G21C 23/00; G21K 5/08; G21D 5/00; G01T 7/02. Claims 3,4,8: G21K 1/00; H02N 1/00; H02K 44/00; G01V 7/00. Claims 3,4,9: G01P 3/50; G01B 11/03; G02B 23/00; H01H 35/02; B65G; B65G 47/22. Claims 3,4,10: G01R 5/00, 33/00; G01J 3/00; G01T; G01W 1/00; G01V 3/00. Claims 3,4,11: G01R 5/00, 33/00; G01J 3/00; G01T; G01W; G01V 1/00, 3/00, 1/104, 1/157; E02B 17/00; E02F. Claims 3,4,12: G21K 1/00, 5/08, 7/00; H02N 1/00.

Unity of invention (S-03 /1998, "Gazette du PCT"). I develop here the New Atomic Scale (Microworld) Physics (instead of the "Einstein-Bohr" Physics of XX century, established by Greatest geniuses) with this "sole general" conception with absolutely (and often opposite) new principal bases and revolutionary (for milliards of years) concrete applications. Evidently such new field (even the new Science!) general invention entitles the new general claims /"... an invention which open up a whole field is entitled to more generally in the claims than one which is concerned with advances in a known technology" ("Guidelines.." §CII-2.2.)). But I guarantee the Unity of Invention also (also) with the help of the discovered New Force in the Atom, conducting futher to the net negation of all basic foundations of the Einstein-Bohr Physics, constructed from beginning of XX century and to the creation of the Absolutely New Atomic scale Physics, with the titanic applications in the sure continuous chain of the sure inventive discoveries, "considered as one whole, relatively to the technical field" where the developed continuous components of these chains (claims) "contain all characteristics of the previous ones" ("Gazette du PCT" S-03/1998 p.48). So the Unity of Invention is made in the double form.

MANY BEST PATENTS OF COMMON MEANS. FITTING TO GIVEN CODES. EASILY TAKEN FROM CD-ROM.

(p.48): a. H01H 35/02, B95G 47/00, B65G 47/22: WO 00/21052, 89/10623, 84/04962, 00/01921, 01/27006; EP:707193, 595446, 813214, 480131, 463291, 253790, 124269, 706028, 305940, 125839, 502248, 124269; FR 2560115, 2519947; 2490197. b, c. G01V (3/00, 1/00), G01W 1/00: WO 01/77712, 00/13647, 01/38903, 00/77755, 00/51093, 95/25966; 01/77702, 01/79873, 99/13358, 98/53345, 98/19750 91/19210; EP 1120629, 718639, 829736, 422895; FR 2779530, 2542453, 2424542, 2670532. G01V 1/104, 1/157, E02F, E02B 17/00: WO 00/63724, 97/48967, 92/11546, 90/13830, 01/79614, EP 1136648, 518427, 1147265. d. G21K 1/00, H02N 1/00, H02K 44/00: WO 00/14750, 00/14759, EP 1112578, 235896. (p.18): G01T 7/02, /04, /06: WO 00/69769, 00/25152; EP 234150, 404681, 008967; FR 2770648, 2729765, 2720506, 2619622.

AMENDED SHEET

with IPEA

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Important supplement for Research- According to the Law.

According to the Law /for instance Art.52(3) of Convention of European Patent Office (EPO)- Administration charged for the International Search/: "The provisions of paragraph 2 (as patentability of discoveries and scientific theories AS SUCH) shall exclude patentability of the subject-matter or activities referred to in that provision only (ONLY) to the extent to which a European patent application.. relates to such... subject-matter or activities as such (it mean without their practical applications)". To see also Accords between EPO and World International Patent Organizatiuon "Gazette du PCT" 56/1997 (Appendix B): "are not excluded from research (PCT) or examination (PCT): all objects that are submitted to the research or examination according to national (European) procedure" Very clearly, as well in "Guidelines for Examination in European Patent Office"- §CIV-2.2.).

This direct stipulation is absolutely EQUIVALENT (since secondary scholl since 12 years old, since "their" Euclide) to the stipulation opposite to the inverse one: "If the European Patent Application concerns the subject-matters (as discoveries and scientific theories) with their applications (= "not as such"), they are patentable ONLY in this case"!

It stipulates clearly according to direct Law /stipulation opposite to the inverse one of Art.52.(3) (EPO)/, these subject-matters (like discoveries and scientific theories) are patentable only with their applications. Consequently, the claims, concerning "Theory or even principle underlining the invention" (letter T according to the Form of the EPO Research (to see also "Guidelines" §CIII-2.2.) and

DECLARATION ABOUT ONLY too simple eliminations from dependent claims of references for several previous claims.

I, Zagyansky Yuly, sole Inventor of Application PCT/EP02/02302, make the following too simple elimination of unneeded references for numerous precedent claims (generally making simple photocopies of published pages).

p.92-40 (line 40) (for claim 3): claim (instead of: claims).

p.93-1 (for claim 3): 1 [instead of: 1(8, 10, 14) and 2].

p.93 (lines 8,9) (for claim 5): claim 1 [instead of: claims 1 (1-5, 8)].

p.96 (lines 7,8) (for claim 7): claim 6 [instead of: claims 1(16), 2 and 6].

p.97-7 (for claim 8): claim 7 [instead of: claims 1, 2, 6 and 8] (also too obvious slip: 7 instead of 8).

p.97 (lines 27, 28) (for claim 9): claim 6 [instead of: claims 1, 2 and 6 (19,20)].

p.98-20 (for claim 11): claim 6 (instead of: claims 1 and 6).

Paris, 11th August 2004. All pages are signed by me verso with date of 08/11/04.

 11 August 2004

receptor cell machinery (of chimpanzee) and the HIV prevent (logically) the 2nd contamination and the AIDS phase (chimpanzee "immunity")

(12) The baby macrophages are more active than that of adult and the baby immune system can already product the antibodies very quickly after the birth, but the 2nd AIDS phase can take place only since ~3 months of age due to the created carbohydrate pattern correspondence between the baby macrophage Fc receptor machinery and HIV virus and, generally, the 2nd contamination can take place due to the very weak transmitted dozes.

(13) The 1st macrophage contamination is made by the macrophage- tropic clones as well the 2nd contamination with also T-cell contaminations, and the T cell- tropic clones provoke the creation of syncytia that undergo the regulated and accelerated apoptosis and the phagocytosis (by macrophages) by the relatively small, almost unvisible, quantities.

(14) Principally, the vaccination must aggravate the contamination due to the antibodies, that help to the contamination, but due to the vaccination with the homogenous envelope proteins, the strong productive contamination is more problematic and these homogenous antibodies can make some decrease of the viral particle quantity (precipitation) and also some blocking of the 1st entry although in the case of the powerful 2nd HIV entry (with CD4 receptor help) there are the dangerous spontaneous re-enterings.

(15) The restricted HIV-2 contaminations take place because of a weaker variability of the viral proteins during the 1st contamination and a stronger differences between the host and virus carbohydrate patterns.

(16) The discrete switching signal due to the specific interactions between the CD4 molecules and the viral envelope proteins, important for AIDS development, are determined by a more general biological molecular processes.

Claim 2. The principal characteristics of the AIDS development process /(a): there is the 1st productive contamination with the cell motility utilisation; (b) the infection increase depends on the antibodies; (c) there is the protein heterogeneity during the 1st contamination, necessary for the heterogenous antibody production, obligatory for 2nd contamination/ according Claim 1 characterized in that a number of other viral Families possesses them.

Claim 3. The viral exterior proteins (envelope or capsule) /Art.52(4) EPO, Art.2(2) AT (law of 1970)/ /for manufacture of medicaments pour vaccinations against viruses (like influenza A-influenza/pneumonia)/ with one (anyway with minimal possible quantity) viral neutralizing epitope and/or one (minimally possible) viral homogenous clone that must be taken for the immunization characterized in that the increase of the virus contaminations is minimal (zero) because the corresponding anti-viral antibodies could increase the cell contaminations with the Fc receptor help wherein the heterogeneity of these antibodies is, generally, obligatory for the virus entry according Claim.

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Claim 4. The substances /Art.52(4) EPO, Art.2(2) AT (law of 1970)/ (for manufacture of medicaments against encephalites), that stop the macrophage motility (as antibodies against the β -chemokine receptors), characterized in that this motility is obligatory for the contaminated macrophage entering into brain to cause the encephalites (as those of CMV origin) according Claim 1

Claim 5. The kit of preparations for the determination of the real titers of the different viruses, with the action, similar to the two HIV phases, according Claims 1

/and Art.52(4) EPO and Art.2(2) AT- law of 1970/ characterized in that for the 1st phase determination: one creates the concentration gradients of the chemokines (as β -chemokines) to switch the macrophage mobility to approach to the conditions of the 1st contamination in vivo, and for the 2nd phase contamination: one utilizes the heterogenous anti-env antibodies (similar to those in vivo) to approach to the conditions of the 2nd contamination in vivo.

Claim 6. The real characteristics of the signalling events that follow the process of the signal switching, produced by the interaction between gp120 and CD4 molecules of the "general process of AIDS development by HIV lentiviruses" of claim 1, are established from the general fundamental processes of the protein foldings and recognitions in the cells, characterized by following characteristics:

(1) There are the chaperon specializations for each glycosylation type: N-, O- and GAG-, that determine the Universal specialities of a limited chaperon number for a protein enormous number by their carbohydrate chains, specialized due to the law of the homologous intercarbohydrate interactions.

(2) There are the two principal pathways of the protein foldings: endoplasmic reticulum→Golgi and in cytoplasm.

(3) The calnexin (chaperon of ER) is monoglycosylated and it is attached to the N-monoglycosylated proteins after the elimination of two other glucoses.

(4) The calnexin makes the complexes with the calreticulin (ER) due to their homologous O-carbohydrates of their similar structures wherein it is the calreticulin that is responsible for the complex with the BiP and grp 94 chaperons later.

(5) During the 1st "trip" in Golgi (ER→Golgi→ER→Golgi), (a) the proteolysis of the terminal N-end (or C- one) (creation of the peptide, named , Du-2T- like) must take place due to the convertases in Golgi; (b) the gag glycosylation must (can) take place.

(6) The creation of the definitive complex, moreover in ER, of the gp96/grp94 chaperon ("boat") with the BiP, calreticulin, p50-like proteins (GAG specificity), peptidyl-prolyl isomerase (PPI) and protein-disulfide isomerase (PDI) (principally) must take place.

(7) The cytoplasmic folding of the polypeptides, yet attached to the ribosomes in cytoplasm, takes place.

hydrogen homologous liaisons between CD4 and gp120 chains already, that is "abated" definitively by the dissociation of the corresponding "Du-2T"-like proteins wherein as a result of the strong conformational change, the other intramolecular liaisons are broken, leading to the agglomerate creations with the membrane melting due to the intercarbohydrate dehydration.

Claim 7. The little proteins (peptides) Du-2T like ("Du-2T") of the synthesized, by ER→Golgi, proteins, including all membranous receptors (as CD4 or gp120) of claim 6 characterized in that they are obtained from N- or C- proprotein ends after the limited proteolysis, they are hidden at the protein surface by the 2 carbohydrate chains with the homologous intercarbohydrate interactions, they are situated near the site of the 2 prolines and S-S bond(s) (source of the irreversible folding with tension) and its dissociation changes the state of the general structure of these proteins profoundly and discretely in liberating the carbohydrate chains for the intermolecular interactions (for formation of the complex aggregate as in the case of the membranous receptors or/and activation of other molecules) like these real little proteins (peptides) for IgG (and also for Fc receptors and receptors for antigen), characterized in that they are situated in the CH2 region and they dissociate after the hapten (antigen) interaction with the active sites because of the consecutive dissociation of the intramolecular coupled interactions of the covering homologous chains in liberating these immunoglobulin chains from already intermolecular interactions: with N-carbohydrate chains of the complement (C1q) (in activating it) or with the carbohydrates of other receptors: Fc and for antigen and with other carbohydrate chains of plasma membrane (PM); like the little real proteins (peptides) (although exceptionally special) Du-2T- like for the molecules MHC class I, characterized in that they are found in "the active site", created by the $\alpha 1$ and $\alpha 2$ domains of the MHC α -chain with the several prolines of these subdomains wherein "the dissociation" of this peptide (Du-2T -like) in the active site of the TRC provokes the strong change of the general structure of the MHC-I α chain, where the sole N-chain carbohydrate (without pair at invariable site) of this subunit can already interact with the corresponding carbohydrate chain (of the invariable site) of the TCR α -chain (also without pair) to switch the "Du-2T" dissociation from the MHC $\alpha 3$ domain with the 2 covering carbohydrate chains, the dissociation, from TCR, of its "Du-2T" (also there is the presence of the prolines, S-S and two symmetric N-carbohydrate chains) (very exceptional presence of the charged amino acids in the intramembranous domains of all components of TCR facilitates the conformational changes due to instability) and the mutual intermolecular interactions of the O- and N- chains of MHC with those of TCR and the CD8 molecules (having own "Du-2T") and between the carbohydrate chains of the same PM (during the complete signal); and like the functional GPI-anchored proteins (so called priones), synthesized by ER→Golgi (in complex aggregate of the classical complete signal) that make the self-aggregation in pathology (diseases

as Mad Cow or Jacob-Creutzfeldt) (this time, without signal already, but like during the signal!), due to the interactions with the forms of these proteins where the "Du-2T" is dissociated already and the carbohydrate chains (hiding) are free for already homologous intermolecular aggregation, facilitating already the dissociation (facilitated also generally!) the dissociation of the "Du-2T" of other molecules.

Claim 8. The large number of the different little proteins (peptides) (Du-2T-like = "Du-2T") according Claim 7 for the manufacture of the medicaments /Art.52(4) EPO, Art.2(2) AT (Law 1970)/ against (1) the undesirable process of the complement activation; (2) the cell lysis; (3) the action of the particular membranous receptors; (4) the action of the parasites as the viruses and also bacteria, protozoans, mushrooms; (5) the creation of the dangerous priones (so called aggregated "scarpie" form) during the diseases as Mad Cow or Creutzfeldt-Jacob; (6) the protein aggregation in solutions (in blood included) characterized in that the simple introduction of these "Du-2T" proteins must stop the corresponding undesirable processes in preventing the dissociation of their native analogues where such dissociation would provoke the harmful signalling including the pathological diseases /(1)-(5)/ or the intermolecular glycoprotein aggregation in solution (6).

Claim 9. The well charged affine molecules (as antibodies) against the distinct HIV surface molecules (or those of other viruses and other parasites like bacteria or mushrooms or against distinct active sites of the surface antibodies, receptors for antigens (B-cells) and/or TCR producing the harmful anti-HIV-env antibodies (or similar harmful antibodies against the other viruses), the harmful auto-antibodies (as anti-HIV-gag or those in rheumatic diseases) or the harmful allergic antibodies, characterized in that these strong, localized precisely, specifically charges perturb the intercarbohydrate homologous hydrogen liaisons of the signalings of HIV and other viruses as well the functioning of the cell, producing these harmful antibodies for manufacture of medicaments /Art.52(4) EPO, Art.2(2) AT (Law 1970)/ according Claim

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Claim 10. The process of the functioning cycle of the cytoplasmic ribosomes for the folding (FKBP type of the proteins for the transporting "PKC" vesicle machinery) and the synthesis of all proteins at all ribosomes according claim 6 is characterized in that (1) During already the signal (in G1 or "G0" or the stocking signal at the G1 end), there is the constitution of the preproribosomes (nucleus, nucleole) from the proteins (with GR peptides), synthesized and folded on the active ribosomes (cytoplasm) (nuclear proteins as nucleolin or fibrillarin or ribosomal proteins as L5 or of the machinery of the transporting "PKC" vesicles /to be stocked/ or the steroid receptors that attach to the rRNA in nucleus /nucleole/); and these preproribosomes are activated (1st step!) by the special signal with the nuclear (serine or cysteine) proteinases (where the proteolysis of the N-part of the nucleolin, attached to the chromatin, is necessary for the pre-rRNA transcription) and they go to the cytoplasm where the 3'

mRNA part serves as the guide for the cytoskeletal localisation; (2) These proribosomes (cytoplasm) are already activated definitively with the cathepsin L (CL) help that cuts (at GR peptides) the particular ribosomal proteins as L5 and the nuclear proteins as the nucleolin and fibrillarin (serving as fusible) and (CL) liberates also the stocked proteins of the "PKC" transporting vesicle machinery (necessary to start again the machinery of the proteins of the "PKC" transporting vesicle cycles without their synthesis) wherein these active ribosomes make the new synthesis and foldings with the help of the corresponding chaperons (FKBP type), attached yet from the nucleus, where, naturally, all ribosomes for all proteins, have the same cycles but without "traveling" proteins with the GR peptides where the same effective process of the protein synthesis of all proteins at the proribosomes (in reality, obtained from the cytoplasm) in vitro (attached for instance on the artificial surfaces) must be made with such CL activation: proribosomes → ribosomes.

Claim 11. The manufactured medicaments /Art.52(4) EPO, Art.2(2) AT law; Accord WIPO-AT/ against the state of the clinical death and coma as phosphatidylinositol-4,5-biphosphate or its derivatives including the lysoderivatives (with easier integration in PM with transport to the interior PM layer) and, like GTP-γS (less hydrolysable substratum also for vesicle transport) characterized in that all these substances help to avoid the process of the irreversible apoptosis of the cells of the brain and heart (original reason of the state of the clinical death and coma) according Claim 6.

Claim 12. The manufactured medicaments (hypnotics) /Art.52(4) EPO, Art.2(2) AT and Accord WIPO-AT) for the partial inhibition of the cycle of the "PKC" and synaptic ("PKC"-like) vesicles (like very deluted cyanate) for the sleep process are characterized in that they cut partially the cyclic system of the neurons of the superior brain (determining the cycle, establishing the conscience), functioning by the chaotic permanent cycles of the synaptic ("PKC"-like) transport vesicles according Claim 6(12).

Abstract.

All AIDS principal mysteries are resolved. "One step" AIDS is successive contaminations (with low [anti-env]). Strong sole lethal animal doses are confirming. Mobility macrophage (mφ) receptors contaminate at 1st stage with nonproductive entry with nonintegrated and heterogenous (due to nef) HIV DNA and proteins and pseudoinfectious A particles. Such heterogeneity is obligatory for 2nd productive contamination with heterogenous anti-env, with integrated DNA and homologous proteins. Encephalites are due to moving into brain mφ due to locally liberated cyto and chemokines. Nongenetic factors are determining: at general persistent seronegativity (contact regularity) or absence of 2nd contamination due to different Fc receptor carbohydrates (babies before 3 months, chimpanzee). Minor genetic factors (as CCR5-2) only modify. AIDS in explaining all dangerous vaccinations. Carbohydrate origin of NK-cell mechanism. Artificial virus culture contaminations. HIV signalings are resolved with general laws of functional recognitions and foldings with help of Universalest "Du-2T"-like peptides and 2 prolyl-isomerases (coupled trans-cis transitions). Chaperons protect proteins against intercarbohydrate aggregations. Prione "scarpie" state is artificial dissociation of their "Du-2T". MHC and TRC allotypes are due to their carbohydrates. Hearts of any cell functioning: "PKC" transporting vesicle cycle and independent direct DNA activation. Apoptosis: irreversibility of preparation of next signal with stock exhaustions. Ribosome cycles. Key proprotein primary structures confirm above data. Consequences of profoundest bases: mφ mobility stopping against encephalites; charged antibodies eliminate viruses, cancer cells and harmful antibody clones (anti-viral ,anti-auto); "Du-2T" eliminates viruses and "Mad Cow"; vaccines from homogenous viruses with one neutralizing epitope and correct virus titres; ribosomal protein synthesis; means against clinical death and coma; perfectest hypnotics.